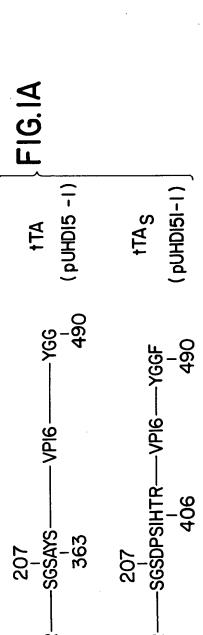
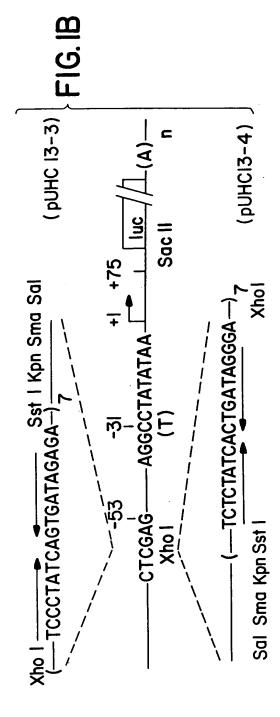
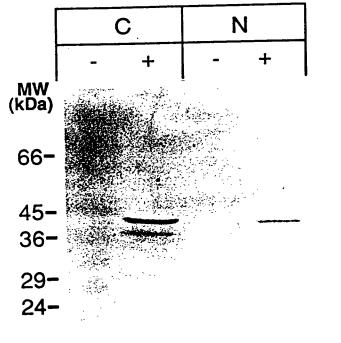
IG.



MSR-





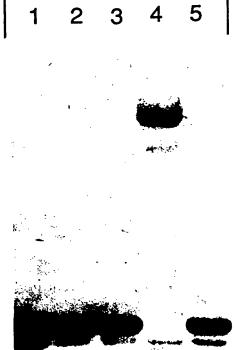
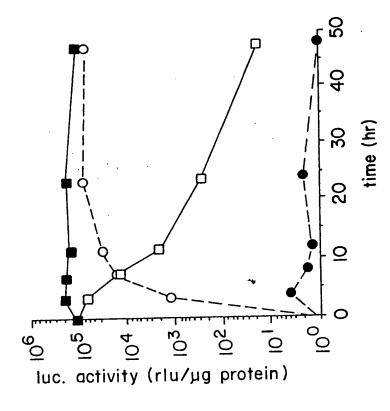


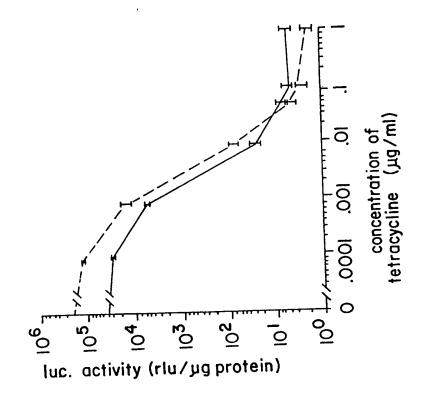
FIG. 2A

FIG. 2B

F16.3A

F16.3B





To Supplie the Council A

Leu Asn GAT AAA AGT AAA GTG ATT AAC AGC GCA TTA GAG CTG CTT AAT Lys Val Ile Asn Ser Ala Leu Glu Leu Leu Asp Lys Ser AGA TTA Arg

Gly Val GGT CTA Len GGA ATC GAA GGT TTA ACA ACC CGT AAA CTC GCC CAG AAG Glu Gly Leu Thr Thr Arg Lys Leu Ala Gln Lys Gly Ile TGG CAT GTA AAA AAT AAG CGG GCT TTG CTC GAC GCC Leu Asp Ala Trp His Val Lys Asn Lys Arg Ala Leu TAT  $\mathtt{T}\mathtt{yr}$ Leu CCT ACA TTG Pro Thr

Glu Gly TGC CCT TTA GAA GGG Len Pro Cys Phe ACT CAC TTT Thr His GCC AIT GAG AIG ITA GAI AGG CAC CAI Leu Asp Arg His His Glu Met Ala Len TIT TIA CGT AAT AAG GCT AAA AGT TIT AGA TGT GCT TIA Phe Arg Cys Ala Leu Ser Phe Leu Arg Asn Lys Ala Lys CAA GAT Gln Asp Trp GAA AGC TGG

Fig. 44

Lys GGT ACA CGG CCT ACA GAA AAA Glu Pro Thr His Arg Asp Gly Ala Lys Val His Leu Gly Thr Arg CAT CGC GAT GGA GCA AAA GTA CAT TTA Ser CTA AGT

Ser CAA GGT TTT Gln Gly Phe Leu Glu Asn Gln Leu Ala Phe Leu Cys Gln TTT TTA TGC CAA TAT GAA ACT CTC GAA AAT CAA TTA GCC Tyr Glu Thr Gln

Cys Ala Val Gly His Phe Thr Leu Gly CTC AGC GCT GTG GGG CAT TTT ACT TTA GGT Leu Ser TTA TAT GCA Leu Tyr Ala GAG AAT GCA Glu Asn Ala CAA GTC GCT AAA GAA GAA AGG GAA ACA CCT Pro Gln Val Ala Lys Glu Glu Arg Glu Thr CAA GAG CAT Gln Glu His GTA TTG GAA GAT Glu Asp Leu

AGT ATG CCG CCA TTA TTA CGA CAA GCT ATC GAA TTA TTT GAT CAC CAA Glu Leu Phe Asp Pro Leu Leu Arg Gln Ala Ile Pro Ser Met

Fig. 4B

CRAST

CCA GCC TIC TIA TIC GGC CII GAA TIG AIC AIA IGC GGA TIA GAA Gly Leu Cys Ile Ile Gly Leu Glu Leu Leu Phe Phe Ala Pro GAG Glu GCA Ala G1y

Asn AAA AAC Thr Lys TAC AGC CGC GCG CGT ACG Ser Arg Ala Arg Glu Ser Gly Ser Ala Tyr \_ 808 GGG ICC CAA CII AAA IGI GAA AGI CysGln Leu Lys Lys

CTC GAT CTC CCG GAC GAC GAC GCC CCC Asp Ala Pro Pro Asp Asp Len Leu Asp ACC ATC GAG GGC CTG Thr Ile Glu Gly Leu Ser GGG GlyTAC  ${
m T}{
m Y}{
m r}$ Asn

GGA CAC ACG His Thr Gly CIC CCC GCG Leu Pro Ala Phe GAG GCG GGG CTG GCG GCT CCG CGC CTG TCT TTT Leù Ala Ala Pro Arg Leu Ser  $_{
m G1y}$ Ala

ACG GCC CCC CCG ACC GAT GTC AGC CTG GGG GAC GAG CTC CAC Glu Leu His Leu Gly Asp Pro Thr Asp Val Ser Thr Ala Pro  ${
m TCG}$ Ser CIG Len Arg Arg

Fig. 4C

iaus i de la fili. Esta launoli Estatum

> TTA GAC GGC GAG GAC GTG GCG ATG GCG CAT GCC GAC GCG CTA GAC GAT TTC GAT His Ala Asp Ala Leu Asp Asp Asp Gly Glu Asp Val Ala Met Ala

Pro His Asp CCG GGA TIT ACC CCC CAC GAC Gly Asp Ser Pro Gly Pro Gly Phe Thr GAC ATG TTG GGG GAC GGG GAT TCC CCG GGT Asp Met Leu Gly Asp

GCC CCC TAC GGC GCT CTG GAT ATG GCC GAC TTC GAG TTT GAG CAG ATG TTT Glu Glu Met Phe Glu Phe Gly Ala Leu Asp Met Ala Asp Phe Ala Pro Tyr Ser

ACC GAT CCC CTT GGA ATT GAC GAG TAC GGT GGG TAG Pro Leu Gly Ile Asp Glu Tyr Gly Gly \*

Fig. 4D

Leu Asp Lys Ser Lys Val Ile Asn Ser Ala Leu Glu Leu Leu Asn ATT AAC AGC GCA TTA GAG CTG CTT AAT TTA GAT AAA AGT AAA GTG TCT AGA Ser Arg

GAA GGT TTA ACA ACC CGT AAA CTC GCC CAG AAG CTA GGT GTA Gly Val Glu Gly Leu Thr Arg Lys Leu Ala Gln Lys Leu GGA ATC Gly Ile TIG TAT IGG CAT GIA AAA AAT AAG CGG GCT TIG CIC GAC GCC Leu Asp Ala Lys Asn Lys Arg Ala Leu Leu Tyr Trp His Val CCT ACA Pro Thr

Glu Gly GAA Leu TIT IGC CCI IIA Pro  $\mathsf{Cys}$ Phe TIA GCC ATT GAG ATG TIA GAT AGG CAC CAT ACT CAC Clu Met Leu Asp Arg His His Thr His Ile Ala

TGG CAA GAT TTT TTA CGT AAT AAC GCT AAA AGT TTT AGA TGT GCT TTA Ser Phe Arg Cys Ala Leu Gln Asp Phe Leu Arg Asn Asn Ala Lys  $\operatorname{Trp}$ Ser

Fig. 54

CGC GAT GGA GCA AAA GTA CAT TTA GGT ACA CGG CCT ACA GAA AAA Glu Lys  $\operatorname{Thr}$ Pro Leu Gly Thr Arg Gly Ala Lys Val His Asp Arg CAT His

Phe Ser Gly Gln Gln TGC CAA CAA Cys Leu TTT TTA Phe CAA TTA GCC Glu Asn Gln Leu Ala CTC GAA AAT Leu Glu Thr GAA ACT  $\operatorname{Tyr}$ 

Leu Gly Cys TTA GGT CTC AGC GCT GTG GGG CAT TTT ACT Phe Thr Ala Val Gly His Leu Ser TAT GCA Tyr Ala Len GCA TTA Asn Ala AAT Glu GAG CAT CAA GTC GCT AAA GAA GAA AGG GAA ACA CCT ACT Glu Thr Glu Glu Arg Lys Gln Val Ala Glu Asp Gln Glu His GAA GAT CAA Leu

His Gln CAC CAA GAT Pro Leu Leu Arg Gln Ala Ile Glu Leu Phe Asp AGT ATG CCG CCA TTA TTA CGA CAA GCT ATC GAA TTA TTT  $\operatorname{Pro}$ Met

Fig. 51

GCA GAG CCA GCC TIC TIA TIC GGC CTT GAA TIG AIC ATA TGC GGA TIA GAA Gly Leu Ile Cys Ten Glu Leu Ile Phe Gly Leu Phe Pro Ala Glu Ala GGT

DOLASS

Len AGA CTG Arg . GGG Arg  $\mathtt{Thr}$ CAC ACG His ATA Ile CCA TCG Pro Ser Asp GAT  $_{
m LCL}$ Gly Ser ტ ტ GAA AGT Cys Glu Ser  $_{
m LGL}$ CTT AAA Gln Leu Lys CAA Lys

CCG ACC GAT GTC AGC CTG GGG GAC GAG CTC CAC TTA GAC GGC Leu Asp Gly Glu Leu His Leu Gly Asp Ser Val Asp Pro Thr Pro ACG GCC CCC Ala  $\operatorname{Thr}$ 

GAC ATG Met Asp Leu CTA GAC GAT TTC GAT CTG Phe Asp Leu Asp Asp Asp Ala GCC GAC GCG Ala His ATG GCG CAT Met Ala GTG GCG Val Ala GAC

GAC GGG GAT TCC CCG GGT CCG GGA TTT ACC CCC CAC GAC TCC GCC CCC Ser Ala His Asp Pro Gly Pro Gly Phe Thr Pro Ser Asp G1yAsp

Fig. 5C

TAC GGC GCT CTG GAT ATG GCC GAC TTC GAG TTT GAG CAG ATG TTT ACC GAT GCC Tyr Gly Ala Leu Asp Met Ala Asp Phe Glu Phe Glu Gln Met Phe Thr Asp Ala

CTT GGA ATT GAC GAG TAC GGT GGG TTC TAG Leu Gly Ile Asp Glu Tyr Gly Gly Phe \* Fig 5D

MAR. 15

CGAGTAGGCGTGTGGGAGGCC<u>TATATAA</u>GCAGAGCTCGTTTAGTGAACCGTCAGATCGC CTGGAGACGCCATCCACGCTGTTTTGACCTCCATAGAAGACACCGGGACCGATCCAGCCTCCGC AAGTCGAGTTTACCACTCCCTATCAGTGATAGAAAAGTGAAAGTCGAGCTCGGTACCCGGGT GAAAGTCGAGTTTACCACTCCCTATCAGTGATAGAGAAAAGTGAAAGTCGAGTTTACCACTCCC TATCAGTGATAGAGAAAAGTCGAGTTTACCACTCCCTATCAGTGATAGAAAAGTGA GAATTCCTCGAGTTTACCACTCCCTATCAGTGATAGAGAAAAGTGAAAGTCGAGTTTACCACTC CCTATCAGTGATAGAGAAAGTGAAAGTCGAGTTTACCACTCCCTATCAGTGATAGAGAAAGT

Fig. 6

r D

CTGGAGACGCCATCCACGCTGTTTTGACCTCCATAGAAGACACCGGGACCGATCCAGCCTCCGC CGAGTAGGCGTGTACGGTGGGAGGCCTATATAAGCAGAGCTCGTTTAGTGAACCGTCAGATCGC CACTGATAGGGAGTGGTAAACTCGACTTTCACTTTTCTCTCTATCACTGATAGGGAGTGGTAAACT ATCACTGATAGGGAGTGGTAAACTCGACTTTCCACTTTTCTCTATCACTGATAGGGAGTGGTAAA CTCGACTTTCACTTTTCTCTATCACTGATAGGGAGTGGTAAACTCGACTTTCACTTTTCTCTAT AACTCGAUTTTCACTTTTCTCTATCACTGATAGGGAGTGGTAAACTCGACTTTCACTTTTCTCT GAATTCCTCGACCCGGGTACCGAGCTCGACTTTCACTTTTCTCTCTATCACTGATAGGGAGTGGTA

Fig. 7

D D DRAF (5°1)

ACGCAGATGCAGTCGGGGCGCGCGGTCCGAGTCCACTTCGCATATTAAGGTGACGCGTGTGG TCGACTTTCACTTTTCTCTATCACTGATAGGGAGTGGTAAACTCGAGATCCGGCGAATTCGAAC TCACTGATAGGGAGTGGTAAACTCGACTTTCACTTTTCTCTATCACTGATAGGGAGTGGTAAAC GAGCTCGACTTTCACTTTTCTCTATCACTGATAGGGAGTGGTAAACTCGACTTTCACTTTTCTC TATCACTGATAGGGAGTGGTAAACTCGACTTTTCACTTTTCTCTCTATCACTGATAGGGAGTGGTAA ACTCGACTTTCACTTTTCTCTATCACTGATAGGGAGTGGTAAACTCGACTTTCACTTTTTTCTCTA CCTCGAACACCGAG

Fig. 8

AGGGGAGCCAGACCTCAGAGGCCTCGTCTGTAGTCTCCGCCATCCCCATCTCCCTGGACGGGTT GGCGCCCCCCCCCCCCACCGAGGTCGGATCCCAGCTCCTGGGTCGCCCGGACCCTGGCCCTTCC GGGAGTT″AGGTCGACATGACTGAGCTGAAGGCAAAGGAACCTCGGGCTCCCCACGTGGCGGGC TCCAGGAGGTGGAGATCCGCGGGTCCAGCCAAACCCCACACACCCATTTTCTCCTCCTTGCCCC GAATTCGAGCTCGGTCCCCCCCCCCTCGAGGTCGACGGTATCGATAAGCTTGATATCGAAT ACGCCATCCACGCTGTTTTGACCTCCATAGAAGACACCGGGACCGATCCAGCCTCCGCGGCCCC GGCGTGTACGGTGGGAGGCCTATATAAGCAGAGCTCGTTTAGTGAACCGTCAGATCGCCTGGAG AGITITACCACTCCCTATCAGTGATAGAGAAAGTGAAAGTCGAGCTCGGTACCCGGGGTCGAGTA TGATAGAGAAAAGTCGAGTTTACCACTCCCTATCAGTGATAGAAAAGTGAAAGTCG CGAGITTACCACTCCCTATCAGTGATAGAGAAAAGTGAAAGTCGAGTTTACCACTCCCTATCAG AGTGATAGAGAAAAGTCGAGTTTACCACTCCCTATCAGTGATAGAGAAAAGTGAAAGT CTCGAGTTTACCACTCCCTATCAGTGATAGAGAAAAGTGAAAGTCGAGTTTACCACTCCCTATC

Fig. 94

AG. SUDDLASS

> GGCCACCGCACCAGGCAGCTGCTGGAGGGGGGGGCTACGACGGCGGGGGCCGCGGCCGCCAGC CGCTTCTCGGCGCCCCAGGGTCTCCTTGGCGGAGCAGGACGCGCCGGTGGCGCCTGGGCGCTCCC CGCTGGCCACCTCGGTGGATTTCATCCACGTGCCCATCCTGCCTCTCAACCACGCTTTCCT AGCTGCCCCCGTCGCGTCTGGAGCGGCCGCAGGAGGCGTCGCCCTTGTCCCCAAGGAAGATTCT GIGAAGCCATCCCCGCAGCCCGCTGCGGTGCAGGTAGACGAGGAGGACAGCTCCGAATCCGAGG GCACCGTGGGCCCGCTCCTGAAGGGCCAACCTCGGGCACTGGGAGGCACGGCGGCCGGAGGAGG CAGGGGACTGTCACCATCCAGGCAGCTGCTCCCCTCCTCTGGGAGCCCTCACTGGCCGGCA TGAGCCGACCCGAGGACAGGCGACAGCTCTGGGACGGCCAGCGGCCCACAAGGTGCTGCC CGAGACCTCCAGAAAAGGACAGCGGCCTGCTGGACAGTGTCCTCGACACGCTCCTGGCGCCCTC GGGTCCCGGGCCAGGCCCAGCCCTGCCACCTGCGAGGCCATCAGCCCGTGGTGCCTGTTT GCTCTTCCCCCGGCCCTGTCAGGGGCAGAACCCCCAGACGGGAAGACGCAGGACCCACGTCG TTGTCAGACGTGGAGGCGCATTTCCTGGAGTCGAAGCCCCGGAGGGGGGCAGGAGACAGCAGCT

Fig. 9B

CCGACTGCACCTACCCGCCCGACGCCCAAAGATGACGCGTTCCCCCTCTACGGCGACTT 

CGIACGIACCTGGTGGTGCAAACCCCGCCGCCTTCCCGGACTTCCAGCTGGCAGCGCCGC

CGCCACCTCGCTGCCGCTCGAGTGCCCTCGTCCAGACCCCGGGGAAGCGGCGGTGGCGGCCTC

CCCAGGCAGTGCCTCCTCCTCCTCGTCGTCGGGGGTCGACCCTGGAGTGCATCCTGTAC

CCGGCGCCTGCCTCCCGCGGGACGGCCTGCCCTCCACCTCCGCCTCGGGCGCGCAGCCGCCGG

GGCCGCCCTGCGCTCTACCCGACGCTCGGCCTCAACGGACTCCCGCAACTCGGCTACCAGGCC

GCCGTGCTCAAGGAGGCCTGCCGCAGGTCTACACGCCCTATCTCAACTACCTGAGGCCGGATT

TGGGGATGAAGCATCAGGCTGTCATTATGGTGTCCTCACCTGTGGGAGCTGTAAGGTCTTCTTT

AAAAGGCCAATGGAAGGCCAGCATAACTATTTATGTGCTGGAAGAAATGACTGCATTGTTGATA

Fig. 9C

H.G. LOCKLASS

TCACAAAACTTCTTGATAACTTGCATGATCTTGTCAAACAACTTCACCTGTACTGCCTGAATAC CTCATCAAGGCAATTGGTTTTGAGGCAAAAAGGAGTTGTTTCCAGCTCACAGCGTTTCTATCAGC CGGATGAAAGAATCATCTATTCACTATGCCTTACCATGTGGCAGATACCGCAGGAGTTTG TCAAGCTTCAAGTTAGCCAAGAAGAGTTCCTCTGCATGAAAGTATTACTACTTCTTAATACAAT TCCTTTGGAAGGACTAAGAAGTCAAAGCCAGTTTGAAGAGATGAGATCAAGCTACATTAGAGAG ATCCTACAAACATGTCAGTGGGCAGATGCTGTATTTTGCACCTGATCTAATATTAAATGAACAG ATGACCAGATAACTCTCCAGTATTCTTGGATGAGTTTAATGGTATTTGGACTAGGATGGAG ACATGACAACACAAGCCTGATACCTCCAGTTCTTTGCTGACGAGTCTTAATCAACTAGGCGAG CGGCAACTTCTTTCAGTGGTAAAATGGTCCAAATCTCTTCCAGGTTTTTCGAAACTTACATATTG TACAGTTAATTCCCCCTCTAATCAACCTGTTAATGAGCATTGAACCAGATGTGATCTATGCAGG CTCCCACAGCCAGTGGGCATTCCAAATGAAAGCCAACGAATCACTTTTTCTCCAAGTCAAGAGA AAATCCGCAGGAAAAACTGCCCGGCGTGTCGCCTTAGAAAGTGCTGTCAAGCTGGCATGGTCCT TGGAGGGCGAAAGTTTAAAAGTTCAATAAAGTCAGAGTCATGAGAGCACTCGATGCTGTTGCT

Fig. 9D

GAGGCAAGACTCGGGCGCCCTGCCCGTCCCACCAGGTCAACAGGCGGTAACCGGCCTCTTC CGACCAAGCTTGGCGAGATTTTCAGGAGCTAAGGAAGCTAAAATGGAGAAAAAAATCACTGGAT ATCGGGAATGCGCGCGACCTTCAGCATCGCCGGCATGTCCCCTGGCGGACGGGAAGTATCAGCT AAAGCAAGTAAAACCTCTACAAATGTGGTATGGCTGATTATGATCCTGCAAGCCTCGTCGTCTG CAGACATGATAAGATACATTGATGAGTTTTGGACAAAACCACAACTAGAATGCAGTGAAAAAAATG CTTTATTTGTGAAATTTGTGATGCTATTGCTTTATTTGTAACCATTATAAGCTGCAATAAACAA AGTTTTTATAATATTCTGAAATTCCTGCAGCCCGGGGGATCCACTAGTTCTAGAGGATC TTATTTTTCAAAGAATTAAGTGTTGTGGTATGTCTTTCGTTTTGGTCAGGATTATGACGTCTCG CAGTTACCCAAGATATTGGCAGGGATGGTGAAACCACTTCTTTTCATAAAAAGTGAATGTCAA ATTTATCCAGTCCCGGGCGCTGAGTGTTGAATTTCCAGAAATGATGTCTGAAGTTATTGCTGCA

Fig. 9E

ORAi 15.

GTCCAACCCGGTAAGACACGACTTATCGCCACTGGCAGCCACTGGTAACAGGATTAGCAGA GGACAGTATTTGGTATCTGCGCTCTGCTGAAGCCAGTTACCTTCGGAAAAAAAGAGTTGGTAGCTC GCGAGGTATGTAGGCGGTGCTACAGAGTTCTTGAAGTGGTGGCCTAACTACGGCTACACTAGAA GGTGGCGAAACCCGACAGGACTATAAAGATACCAGGCGTTTCCCCCTGGAAGCTCCCTCGTGCG CTCTCCTGTTCCGACCCTGCCGCTTACCGGATACCTGTCCGCCTTTCTCCCTTCGGGAAGCGTG GCGCTTTCTCAATGCTCACGCTGTAGGTATCTCAGTTCGGTGTAGGTCGTTCGCTCCAAGCTGG GCTGTGTGCACGAACCCCCCCGTTCAGCCCGACCGCTGCGCCTTATCCGGGTAACTATCGTCTTGA CGCAGGAAAGAACATGTGAGCCAAAAGGCCAGCAAAAGGCCCAGGAACCGTAAAAAGGCCGCGTTG CTGGCGTTTTTCCATAGGCTCCGCCCCCTGACGAGCATCACAAAAATCGACGCTCAAGTCAGA TCAATGTACCTATAACCAGACCGTTCAGCTGCATTAATGAATCGGCCAACGCGGGGGGAGAGGC GGTTTGCGTATTGGGCGCTCTTCCGCTTCGCTCACTGACTCGCTGCGCTCGGTCGTTCGGC TGCGGCGAGCGGTATCAGCTCACTCAAAGGCGGTAATACGGTTATCCACAGAATCAGGGGATAA

Fig. 9F

TGTCATGCCATCCGTAAGATGCTTTTCTGTGACTGGTGAGTACTCAACCAAGTCATTCTGAGAA TAGTGTATGCGGCGACCGAGTTGCTCTTGCCCGGCGTCAATACGGGGATAATACCGCGCCACATA CGAGTTACATGATCCCCCATGTTGTGCAAAAAAGCGGTTAGCTCCTTCGGTCCTCCGATCGTTG TCAGAAGTAAGTTGGCCGCAGTGTTATCACTCATGGTTATGGCAGCACTGCATAATTCTCTTAC GGGAAGCTAGAGTAGTTCGCCAGTTAATAGTTTGCGCAACGTTGTTGCCATTGCTACAGG CCTGACTCCCCGTCGTAGATAACTACGATACGGGAGGGCTTACCATCTGGCCCCCAGTGCTGC TACCAATGCTTAATCAGTGAGGCACCTATCTCAGCGATCTGTCTATTTCGTTCATCCATAGTTG TITAAATTAAAATGAAGTTTTAAATCAATCTAAAGTATATATGAGTAAACTTGGTCTGACAGT ACGAAAACTCACGTTAAGGGATTTTGGTCATGAGATTATCAAAAAGGATCTTCACCTAGATCCT CGCAGAAAAAAAGGATCTCAAGAAGATCCTTTGATCTTTTCTACGGGGTCTGACGCTCAGTGGA

Fig. 9G

CCGCGCACATTTCCCCCGAAAGTGCCACCTGACGTCTAAGAAACCATTATTATCATGACATTAA ACTITICACCAGCGTTTCTGGGTGAGCAAAACAGGAAGGCAAAAATGCCGCAAAAAAGGGAATAA GGGCGACACGGAAATGTTGAATACTCATACTCTTCCTTTTTCAATATTTGAAGCATTTATCA GGGTTATTGTCTCATGAGCGGATACATATTTGAATGTATTTAGAAAAAAATAAACAAATAGGGGTT ACCGCTGTTGAGATCCAGTTCGATGTAACCCACTCGTGCACCCAACTGATCTTCAGCATCTTTT

CCTATAAAAATAGGCGTATCACGAGGCCCTTTCGTC

Fig. 9H

AGCGTGTCTCCGAGCCCGCTGATGCTACTGCACCCGCCGCCGCAGCTGTCGCCTTTCCTGCAGC CGGCCCCGGGTCTGAGGCTGCGGCGTTCCAACGGCCTGGGGGGTTTCCCCCCCACTCAAC CCTACGAGTTCAACGCCGCCGCCGCCAACGCGCAGGTCTACGGTCAGACCGGCCTCCCTA TCAGATCCAAGGGAACGAGCTGGAGCCCCTGAACCGTCCGCAGCTCAAGATCCCCCTGGAGCGG CCCCTGGGCGAGGTGTACCTGGACAGCAAGCCCGCCGTGTACAACTACCCCGAGGGCGCCG GAATTCCGCCCACGACCATGACCCTCCACACCAAAGCATCTGGGATGGCCCTACTGCA ACGCCATCCACGCTGTTTTGACCTCCATAGAAGACACCGGGACCGATCCAGCCTCCGCGGCCCC AGITITACCACTCCCTATCAGTGATAGAGAAAAGTGAAAGTCGAGCTCGGTACCCGGGTCGAGTA GGCGTGTACGGAGGCCTATATAAGCAGAGCTCGTTTAGTGAACCGTCAGATCGCCTGGAG TGATAGAGAAAAGTGAAGTCGAGTTTACCACTCCCTATCAGTGATAGAGAAAAGTGAAAGTCG CGAGITTACCACTCCCTATCAGTGATAGAGAAAAGTGAAAGTCGAGTTTACCACTCCCTATCAG CTCGAGTTTACCACTCCCTATCAGTGATAGAGAAAAGTGAAAGTCGAGTTTACCACTCCCTATC AGTGATAGAGAAAAGTCGAGTTTACCACTCCCTATCAGTGATAGAGAAAAGTGAAAGT

Fig. 10A

DRAFTS.

ATCAACTGGGCGAAGAGGGTGCCAGGCTTTGTGGATTTGACCCTCCATGATCAGGTCCACCTTC TAGAATGTGCCTGGCTAGAGATCCTGATGATTGGTCTCGTCTGGCGCTCCATGGAGCACCCAGT TGGTCATGGCCTTGGATGCTGAGCCCCCCATACTCTATTCCGAGTATGATCCTACCAGACC CTTCAGTGAAGCTTCGATGATGGGCTTACTGACCAACCTGGCAGACAGGGAGCTGGTTCACATG TGATGGGGAGGGCAGGGGTGAAGTGGGGGTCTGGAGACATGAGAGCTGCCAACCTTTGGCCA AGCCCGCTCATGATCAAACGCTCTAAGAAGAACAGCCTGGCCTTGTCCCTGACGGCCGACCAGA TGAAAGGTGGGATACGAAAAGACCGAAGAGGGGAGAATGTTGAAACACACAAGCGCCAGAGAGA GATAAAAACAGGAGGAAGAGCTGCCAGGCCTGCCGGCTCCGCAAATGCTACGAAGTGGGAATGA GCCAGTACCAATGACAAGGGAAGTATGGCTATGGAATCTGCCAAGGAGACTCGCTACTGTGCAG TGTGCAATGACTATGCTTCAGGCTACCATTATGGAGTCTGGTCTGTGAGGGCTGCAAGGCCTT CCCACGGCCAGGTGCCCTACTACCTGGAGAACGAGCCCAGCGGCTACACGGTGCGCGAGGC CGGCCCGCCGCCATTCTACAGGCCAAATTCAGATAATCGACGCCAGGGTGGCAGAGAAAGATTG

Fig. 10B

10.

CTTTATTTGTGAAATTTGTGATGCTATTGCTTTATTTGTAACCATTATAAGCTGCAATAAACAA CAGACATGATAAGATACATTGATGAGTTTTGGACAAAACCACAACTAGAATGCAGTGAAAAAAATG TGCCACAGAGTCTGAGAGCTCCCTGGCGGAATTCGAGCTCGGTACCCCGGGGATCCTCTAGAGGATC TCCTCCTCCTCTCCCACACATCAGGCACATGAGTAACAAAGGCATGGAGCATCTGTACAGCAT GAAGTGCAAGAACGTGGTGCCCCCTCTATGACCTGCTGCTGGAGATGCTGGACGCCCACCGCCTA TTGATCCACCTGATGGCCAAGGCCAGGCCTGACCCTGCAGCAGCAGCAGCAGCGGCTGGCCCAGC AGGAGTTTGTGTGCCTCAAATCTATTTTTGCTTAATTCTGGAGTGTACACATTTCTGTCCAG GTGGAGATCTTCGACATGCTGCTGGCTACATCTCGGTTCCGCATGATGAATCTGCAGGGAG CACCCTGAAGTCTCTGGAAGAAGGACCATATCCACCGAGTCCTGGACAAGATCACAGACACT GAAGCTACTGTTTGCTCCTAACTTGCTCTTGGACAGGAAACCAGGGAAAATGTGTAGAGGGCATG

Fig. 10C

ACTOR TO THE STATE OF THE STATE

CTCTCCTGTTCCGACCCTGCCGCTTACCGGATACCTGTCCGCCTTTCTCCCTTCGGGAAGCGTG CTGGCGT1 TTTCCATAGGCTCCGCCCCCTGACGAGCATCACAAAATCGACGCTCAAGTCAGA GGTGGCGAAACCCGACAGGACTATAAAGATACCAGGCGTTTCCCCCCTGGAAGCTCCCTCGTGCG CGCAGGAAAGAACATGTGAGCCAAAAAGGCCAAGGCCAGGAACCGTAAAAAGGCCGCGTTG TGCGGCGAGCGGTATCAGCTCACTCAAAGGCGGTAATACGGTTATCCACAGAATCAGGGGATAA TCAATGTACCTATAACCAGACCGTTCAGCTGCATTAATGAATCGGCCAACGCGGGGGGAGGGC GGTTTGCGTATTGGGCGCTCTTCCGCTCGCTCACTGACTCGCTGCGCTCGGTCGTTCGGC CGACCAAGCTTGGCGAGATTTTCAGGAGCTAAGGAAAAAATGGAGAAAAAATCACTGGAT GAGGCAAGACTCGGGCGCGCCCTGCCCGTCCCACCAGGTCAACAGGCGGTAACCGGCCTCTTC ATCGGGAATGCGCGCGCCTTCAGCATCGCCGGCATGTCCCCTGGCGGACGGGAAGTATCAGCT AAAGCAAGTAAAACCTCTACAAATGTGGTATGGCTGATTATGATCCTGCAAGCCTCGTCGTCTG

Fig. 10D

GCGCTTTCTCAATGCTCACGCTGTAGGTATCTCAGTTCGGTGTAGGTCGTTCGCTCCAAGCTGG GCTGTGTGCACGAACCCCCCGTTCAGCCCGACCGCTGCGCCTTATCCGGTAACTATCGTTTGA

TACCAATGCTTAATCAGTGAGGCACCTATCTCAGCGATCTGTCTATTTCGTTCATCCATAGTTG CCTGATCCCCGTCGTGGATAACTACGATACGGGAGGGCTTACCATCTGGCCCCAGTGCTGCA TITAAATTAAAATGAAGTTTTAAATCAATCTAAAGTATATATGAGTAAACTTGGTCTGACAGT CGCAGAAAAAAAGGATCTCAAGAAGATCCTTTGATCTTTTCTACGGGGTCTGACGCTCAGTGGA ACGAAAACTCACGTTAAGGGATTTTGGTCATGAGATTATCAAAAAGGATCTTCACCTAGATCCT GCGAGGTATGTAGGCGGTGCTACAGAGTTCTTGAAGTGGTGGCCTAACTACGGCTACACTAGAA GGACAGTATTTGGTATCTGCGCTCTGCTGAAGCCAGTTACCTTCGGAAAAAAAGTTGGTAGCTC GTCCAACCCGGTAAGACACGACTTATCGCCACTGGCAGCAGCCACTGGTAACAGGATTAGCAGA

Fig. 10E

CGCGCACATTTCCCCCGAAAAGTGCCACCTGACGTCTAAGAAACCATTATTATCATGACATTAAC GGCGACACGGAAATGTTGAATACTCTTCCTTTTTTTCAATATTTGAAGCATTTATCAG CCGCTGTTGAGATCCAGTTCGATGTAACCCACTCGTGCACCCAACTGATCTTCAGCATCTTTA CTTTCACCAGCGTTTCTGGGTGAGCAAAAACAGGAAGGCAAAAATGCCGCAAAAAAGGGAATAAG AGTGTATGCGGCGACCGAGTTGCTTTGCCCGGCGTCAATACGGGGATAATACCGCGCCACATAG CAGAACTTTAAAAGTGCTCATCATTGGAAAACGTTCTTCGGGGCGAAAACTCTCTAAGGATCTTA CAGAAGTAAGTTGGCCGCAGTGTTATCACTCATGGTTATGGCAGCACTGCATAATTCTCTTACT GTCATGCCATCCGTAAGATGCTTTTCTGTGACTGGTGAGTACTCAACCAAGTCATTCTGAGAAT GAGTTACATGATCCCCCATGTTGTGCAAAAAAGCGGTTAGCTCCTTCGGTCCTCCGATCGTTGT GGAAGCTPGAGTAAGTTCGCCAGTTAATAGTTTGCGCAACGTTGTTGCCATTGCTACAGGC CTATAAAAATAGGCGTATCACGAGGCCCTTTCGTC

Fig. 10F

FIG. II

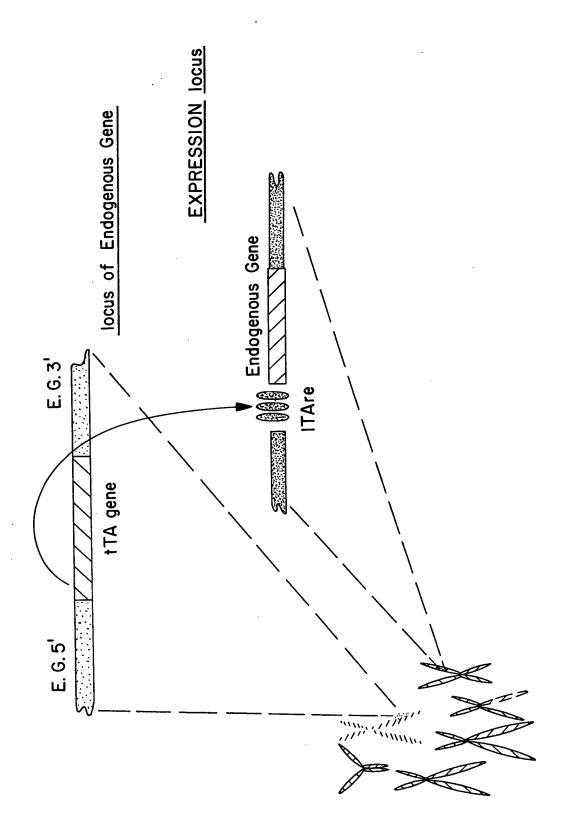
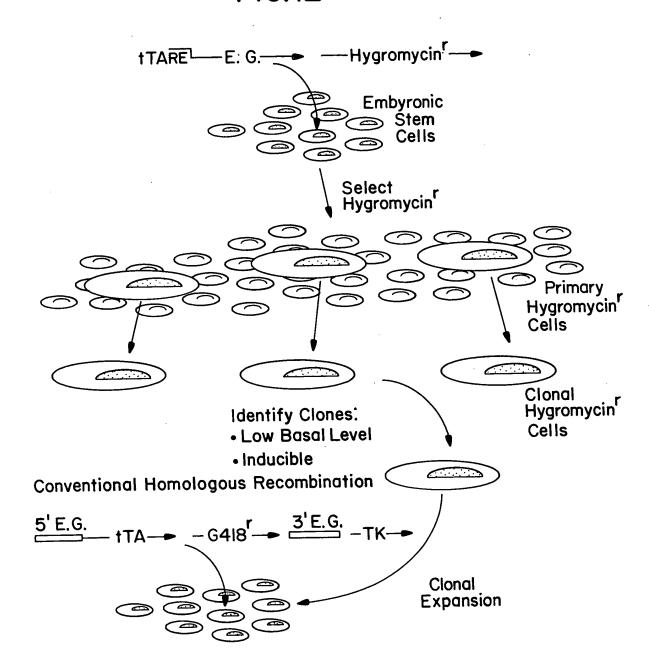


FIG. 12



F16.13A

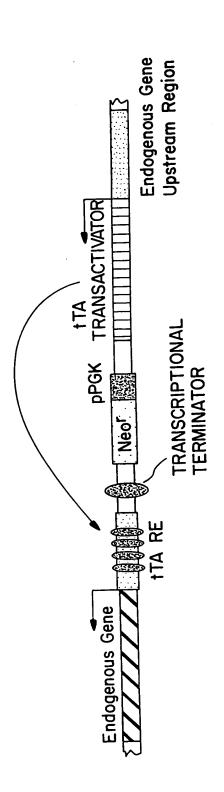
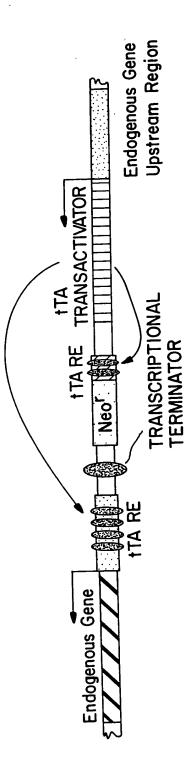
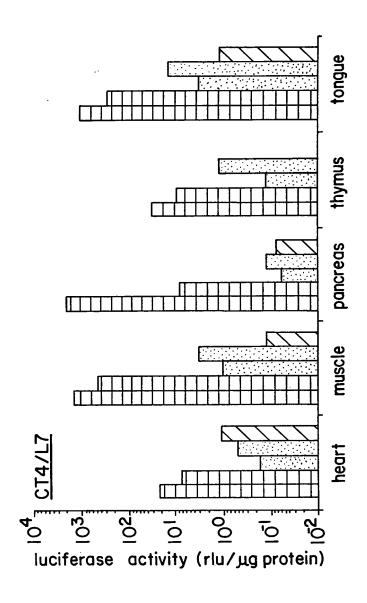


FIG. 13B



DRAFi:

F16.14



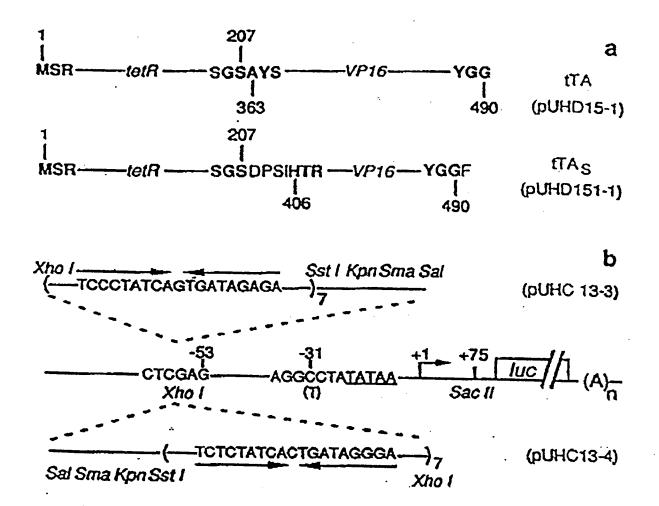


Fig. I

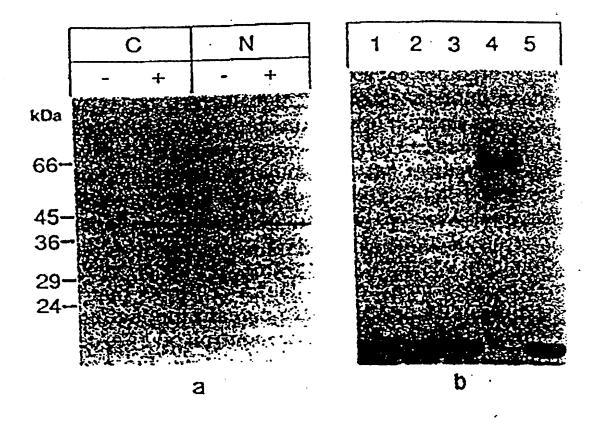


Fig. 2

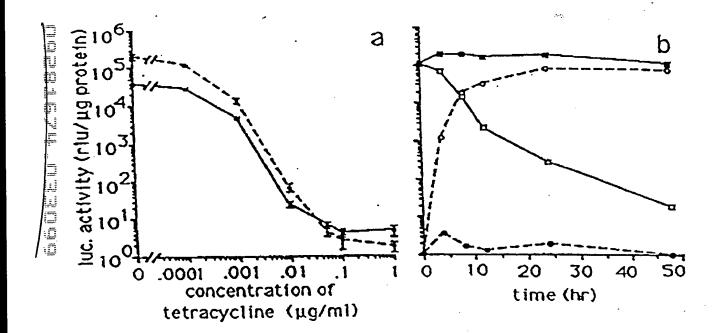


Fig. 3

31/11 ATG TOT AGA TEA GAT AAA AGT AAA OTG ATT AAG AGG GCA TEA GAG CTG CTT AAT GAG GTG Met ser any leu asp lys ser lys wal ile asm ser ala leu giu leu asm glu wal COA ATC CAR OUT TEX ACR ACC COT ANA CTC GCC CAG ANG CTA GCT GEN CAG CAG CCT ACR Gly 11e glu gly leu thr thr any lys leu sla glu lys leu gly val glu glu pro thr 121/41 91/31 TTG TAT TOG CAT GTA ARA ART ARG COO GCT TTG CTC CAG CCC TTA GCC ATT CAG ATG TTA leu tyr trp his val lys asn lys ary als leu leu asp als leu als ile glu met leu 181/61 CAT AGG CAC CAT ACT CAC TIT TOO COT TEA GAA GOG CAA AGC TOG CAA CAT TIT TIA CCT amp and his his the his phe cys pro led glu gly glu sor trp glu amp phe led and 271/91 241/81 ARE AND OUT ANA NOT TIT AGA TOT OUT THA CITA AGT CAT OSC CAT GOA GOA ANA GITA CAT son lys als lys ser phe arg cys als lou leu ser his ary asp gly als lys val his 331/111 THA GGT ACA CGG CCT ACA GAA AAA CAG TAT GAA ACT CTC GAA AAT CAA TIA GCC TIT TTA 301/101 led gly the arg pro the glu lys gln tyr glu the led glu am gln led ala phe led 391/131 361/121 451/151 ACT THE GOT TOC OTH THE GRA CAT CAN CAC CAT CAR OTC GOT ARE CAR CAR AGE CAR ACE thr leu gly cys wal leu glu asp gin glu his gin wal she lye glu glu arg glu thr \$11/171 481/161 OUT ACT ACT OAT ACT ATG COG OCA THA THA OSA CHA OCT ATC CAR THA THE GAT CAC CAR pro thr the asp ser met pro pro leu leu ary gln ala ile glu leu phe aep his gln \$41/181 GOT GOA GAG GOA GOC TIC TIA TIC GGC CIT GAN TIG ATC ATA TOC GOA TIA GAN ANA CAN gly ala glu pro als phe leu phe gly lou glu leu ile ile cys gly lou glu lys glu 631/211 601/201 CIT ANA TOT GAN ACT OCC TOC GOO TAC ACC GOO GOO GOT ACC ANA AAC AAT THE GOO TOT leu lys cys giu ser gly ser ala tyr ser arg ala arg thr lys ann sen tyr gly ser 661/221 661/221 ACC ATC GAG GGC CTC CAT CTC CCG GAC GAC GAC GGC GCC CAA GAG GCG GGG CTG GCG thr ile glu gly leu leu asp lou pro asp asp asp ala pro glu glu ala gly leu ala 721/241 GCT CGG CGC CTG TCC TTT CTC CCC GCG GGA CAC ACG CGC ACA CTG TCG ACG GCC CCC CCC als pro arg leu ser phe leu pro als gly his thr arg arg leu ser thr als pro pro 781/261 ACC CAT GIC AGC CITG GGG GAC CAG CITC CAC TITA GAC GGC GAG GAC GTG GGG ATC GGG CAT thr asp wal ser led gly sep glu led his led asp gly glu asp wal als met als his 841/381 QCC CAC CCC CTA CAC CAT TTC GAT CTG CAC ATC TTG CEG CAC CGG CAT TCC CCG CGT CCC als asp als leu asp asp phe asp leu asp met leu gly asp gly asp ser pro gly pro 931/311 901/301 CON THE ACC CON CAR CAR TON COR COR THE COS COT CTG CAR ATC COR CAR THE CAR THE gly plue the pro his amp eer als pro tyr gly als leu amp met als sep plue glu plue 991/331 CAG CAG ATC TIT ACC GAT COC CIT GGA ATT CAC CAG TAC GGT GGG TAG glu gin met phe thr sep pro leu gly ile asp glu tyr gly gly AMB

31/13 ATO TOT AGA TEA GAT AAA AGT AAA GTG ATT AAC AGC GCA TEA GAG CTG CTT AAT GAG GTC Met ser arg leu asp lys ser lys val 11e sen ser ala leu glu leu leu esn glu val GGA ATC CAA GOT WIM ACA ACC COT MAN CTC CCC CAG ANG CTA CCT GTA CAG CAG CCT ACA GIV 110 glu gly leu thr thr are lys leu als gln lys leu gly val glu gln pro thr 121/41 91/31 THE TAT YOU CAT GIA ANA NAT AND COS OCT THE CTC CAC GOO THA GOO ANT GAS ATE THA Lou byr try his val lys ass lys any ala leu leu asp ala leu ala ile glu met leu 211/71 GAT AGG CAC CAT ACT CAC TIT TOC CCT TTA GAA GGG GAA AGC TGG CAA GAT TIT TTA CCT asp any his his thr his phe cys pro leu glu gly glu eer trp gln asp pha leu arg 271/91 241/81 ART ARC GOT ARA ACT TIT ACK TOT COT THE CTA ACT CRY COC GAT COR OCK ARA CTA CAT ash ash als lye ser phe any cys ale led led ser his any asp gly als lye wal his 331/111 THE GOT ACK COG COT ACK CAN AND CAG THE GAN ACT COT CAN ART CAN THE GOO THE TIM 301/101 led gly thr are pro thr glu lys gln tyr glu thr led glu asn gln led als phe lod 391/131 THE CAN CAN GOT THE TEX CEN CAN ANT OCH THE TAT OCH CHE AGE OCT ONE GOO CAT THE 361/121 cys gln gln gly phe ser leu glu asn sla leu tyr ala leu ser ala vel gly his phe 421/141 ACT TIN GOT TOC OTA TITE CAN CAT CAN GRE CAT CAN GIC GCT ARA GAN GAN AGG GAN ACA thr leu gly eye wal leu glu sep gla glu his gla wal ale lys glu giu erg glu thr 511/171 481/161 COT ACT ACT CAT ACT ATC COG COA TTA TTA COA CAA GOT ATC CAA TTA TAT CAS CAC CAA pro the the asp see met pro pro leu leu arg gln als ile glu leu phe asp his gln 571/191 COT COA CAG COA COC TTC TOA TTC COC CIT CAN TTC ATA TOC COA TTA CAN ANA CAN gly ala glu pro ala phe Lau phe gly leu glu leu ile ile cya gly leu glu lyc glp 631/211 601/201 CIT AND TOT GAN AND GOO TOT GAT OUR TOG ATH CAC MOG COC AGA CITO TOG ACG GOO COC leu lys cys glu ser gly ser asp pro ser ile his thr arg erg leu ser thr ala pro 691/231 COS AGO CAT GTC AGO CTG GGG CAC CAG CTC CAC TTA GAC GGC CAG GAC GTG GCG ATG GCG pro thr asp wal ser leu gly asp glu leu his leu asp gly glu asp wal ala met ala 751/25% CHT GOC GAC GCG CTA GAC GAT TTC GAT CTC GAC ATC TTG GGG GAC GGG GAT TGC GGG GAT his als asp als led sep sep phe asp led sep mot led gly sep ger pro gly 811/271 781/261 OCE OUR TITE ACC COC CAC CAC TOC COC CUE TAC OCC COT CTO CAT ATG OUC GAC TTC CAG pro gly phe thr pro his asp ser als pro tyr gly als leu asp met als asp phe glu 871/291 841/281 TIT GAG CAG ATG TIT ACC CAT GCC CIT GGA ATT CAC CAG TAC CCT GCC TIC TAC phe glu gln met phe thr asp ala lou gly ile asp glu tyr gly gly phe AMB

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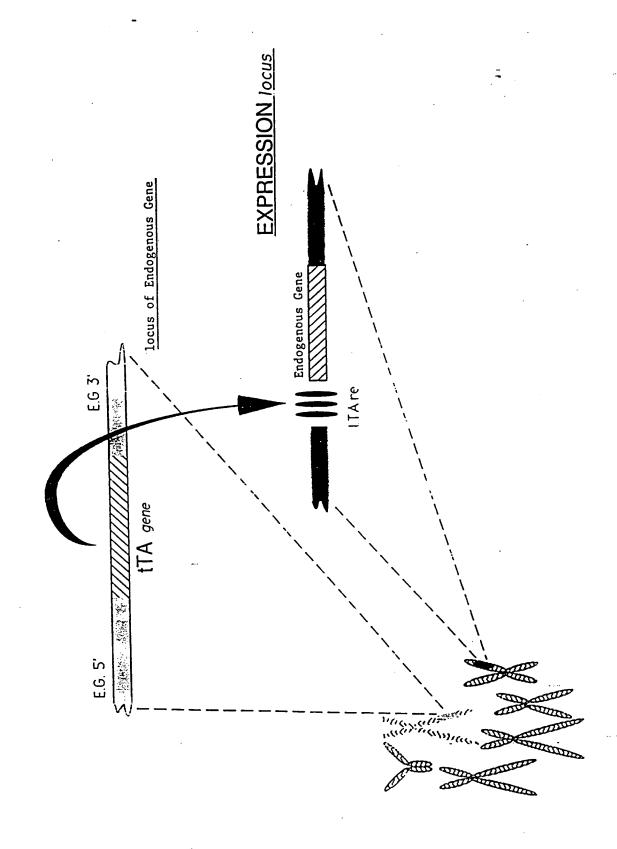
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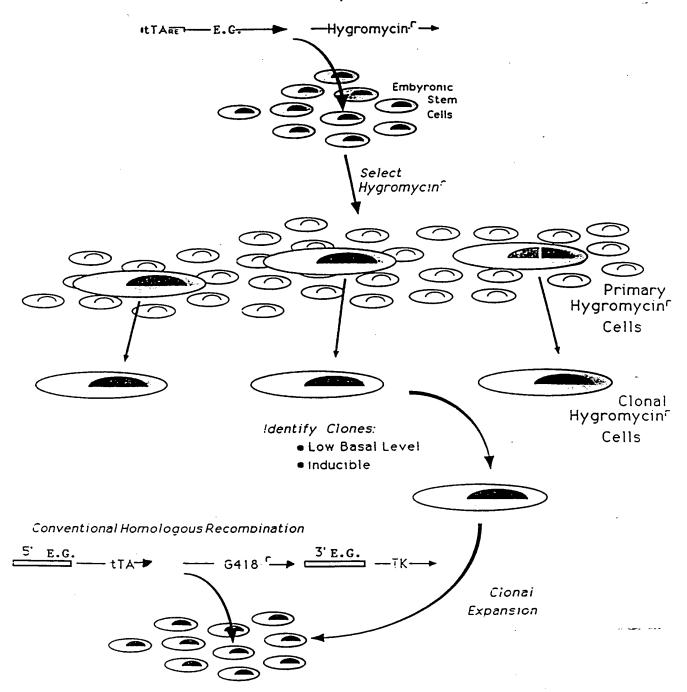
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## Conditional Knock-Out Strategy 1



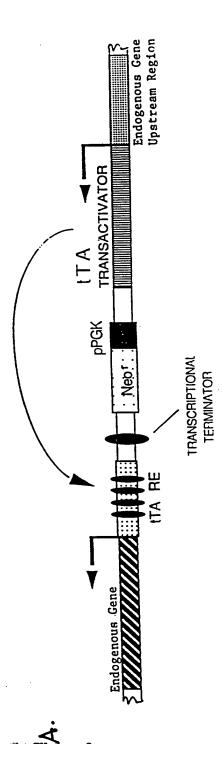
Conditional Knock-Out Strategy 2



Identify clones with low basal activity of endogenous gene (near untransformed levels). Identify among these those which respond to tTA (by transient expression).

Perform homologous recombination into endogenous locus.

## Conditional Knock-Out Strategy 3



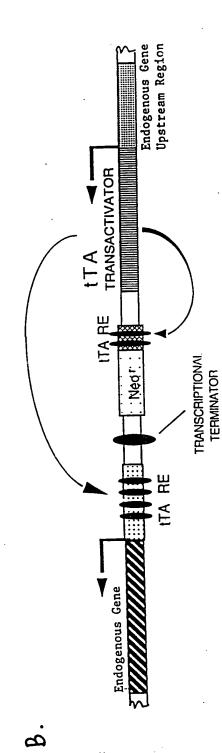


Figure 14